

What is claimed is:

- 1 1. A method for identifying multiple different activated transcription factors in
2 a cell sample, the method comprising:
3 transducing or transfecting a cell sample to comprise a library of constructs,
4 each construct comprising
5 a cis element sequence comprising one or more copies of a cis
6 element to which a transcription factor is capable of binding, the cis element
7 sequence varying within the library of constructs,
8 a promoter sequence 3' relative to the cis element sequence, and
9 a reporter sequence 3' relative to the promoter sequence that
10 comprises a variable sequence that varies within the library,
11 wherein a same cis element sequence is employed with a given
12 reporter sequence within the library of constructs;
13 forming mRNA transcription products by those of the transduced or
14 transfected cells in which an activated transcription factor is present that binds to the
15 cis element of the construct present in the cell and activates transcription of the
16 reporter sequence of the construct present in the cell;
17 determining which reporter sequences are comprised within the mRNA
18 transcription products; and
19 determining which activated transcription factors are present in the cell
20 sample based on which reporter sequences were transcribed.
- 1 2. A method according to claim 1 wherein the library of cells comprises at least
2 10 different cis elements.
- 1 3. A method according to claim 1 wherein the library of cells comprises at least
2 20 different cis elements.
- 1 4. A method according to claim 1 wherein the library of cells comprises at least
2 50 different cis elements.

1 5. A method according to claim 1 wherein the library of cells comprises at least
2 100 different cis elements.

1 6. A method according to claim 1 wherein the cis element sequence comprises
2 at least two copies of the cis element.

1 7. A method according to claim 1 wherein the cis element sequence comprises
2 at least three copies of the cis element.

1 8. A method according to claim 1 wherein the cis element sequence comprises
2 at least four copies of the cis element.

1 9. A method according to claim 1 wherein an individual copy of the cis element
2 has a length between about 5 and 100 base pairs.

1 10. A method according to claim 1 wherein an individual copy of the cis element
2 has a length between about 5 and 75 base pairs.

1 11. A method according to claim 1 wherein an individual copy of the cis element
2 has a length between about 5 and 50 base pairs.

1 12. A method according to claim 1 wherein the variable sequence of the reporter
2 sequence is at least 15 bases in length.

1 13. A method according to claim 1 wherein the variable sequence of the reporter
2 sequence is at least 25 bases in length.

1 14. A method according to claim 1 wherein the variable sequence of the reporter
2 sequence is at least 50 bases in length.

1 15. A method according to claim 1 wherein the variable sequence of the reporter
2 sequence is between 15 and 2000 bases in length.

1 16. A method according to claim 1 wherein the variable sequence of the reporter
2 sequence is between 25 and 2000 bases in length.

1 17. A method according to claim 1 wherein the variable sequence of the reporter
2 sequence is between 50 and 2000 bases in length.

1 18. A method according to claim 1 wherein the cell sample comprises
2 mammalian cells.

1 19. A method according to claim 1 wherein the cell sample was obtained from a
2 human.

1 20. A method according to claim 1 wherein determining which activated
2 transcription factors are present in the cell sample based on which reporter
3 sequences were transcribed comprises using a look-up table to correlate transcribed
4 reporter sequences with activated transcription factors.

1 21. A method according to claim 20 wherein the library of cells comprises at
2 least 10 different reporter sequences.

1 22. A method according to claim 20 wherein the library of cells comprises at
2 least 20 different reporter sequences.

1 23. A method according to claim 20 wherein the library of cells comprises at
2 least 50 different reporter sequences.

1 24. A method according to claim 1 wherein determining which of the reporter
2 sequences were transcribed comprises reverse transcribing the mRNA transcription
3 products to form cDNA and determining which of the reporter sequences or
4 compliments thereof are comprised within the cDNA.

- 1 25. A method according to claim 24 wherein the reporter sequences comprise
2 priming sequences 5' and 3' relative to the variable sequences, the method further
3 comprising amplifying the cDNA.
- 1 26. A method according to claim 24 wherein determining which of the reporter
2 sequences or compliments thereof are comprised within the cDNA comprises
3 sequencing the cDNA.
- 1 27. A method according to claim 24 wherein determining which of the reporter
2 sequences or compliments thereof are comprised within the cDNA comprises
3 performing a hybridization assay using a library of hybridization probes to detect the
4 reporter sequences and/or compliments thereof.
- 1 28. A method according to claim 27 wherein the library of hybridization probes
2 are immobilized in an array.
- 1 29. A method according to claim 1 wherein the reporter sequences encode
2 reporter proteins which the cells express from the mRNA transcription products,
3 determining which reporter sequences are comprised within the mRNA transcription
4 products comprising determining which of the reporter proteins were expressed.
- 1 30. A method according to claim 29 wherein determining which of the reporter
2 proteins were expressed comprises employing a library of antibodies capable of
3 binding to the reporter proteins to detect the expressed reporter proteins.
- 1 31. A method according to claim 30 wherein the library of antibodies are
2 immobilized in an array.
- 1 32. A method for characterizing a cell type of a cell sample, the method
2 comprising:
3 identifying multiple different activated transcription factors in a cell sample
4 by

5 transducing or transfecting a cell sample to comprise a library of
6 constructs, each construct comprising
7 a cis element sequence comprising one or more copies of a cis
8 element to which a transcription factor is capable of binding, the cis element
9 sequence varying within the library of constructs,
10 a promoter sequence 3' relative to the cis element sequence,
11 and
12 a reporter sequence 3' relative to the promoter sequence that
13 comprises a variable sequence that varies within the library,
14 wherein a same cis element sequence is employed with a
15 given reporter sequence within the library of constructs,
16 forming mRNA transcription products by those of the transduced or
17 transfected cells in which an activated transcription factor is present that binds to the
18 cis element of the construct present in the cell and activates transcription of the
19 reporter sequence of the construct present in the cell,
20 determining which reporter sequences are comprised within the
21 mRNA transcription products, and
22 determining which activated transcription factors are present in the
23 cell sample based on which reporter sequences were transcribed; and
24 using the combination of multiple different activated transcription factors
25 identified as being present in a cell sample to identify the cell type of the cell
26 sample.

1 33. A method according to claim 32, wherein using the identified combination of
2 multiple different activated transcription factors comprises comparing the identified
3 combination of multiple different activated transcription factors to combinations of
4 different activated transcription factors known to be present in known cell types.

1 34. A method according to claim 33, wherein the known cell types comprise
2 diseased and/or healthy cells of a given cell type.

1 35. A method according to claim 33, wherein the combinations of different
2 activated transcription factors present in known cell types are determined by
3 transducing or transfecting a cell sample of a known cell type to comprise a
4 library of constructs, each construct comprising
5 a cis element sequence comprising one or more copies of a cis
6 element to which a transcription factor is capable of binding, the cis element
7 sequence varying within the library of constructs,
8 a promoter sequence 3' relative to the cis element sequence, and
9 a reporter sequence 3' relative to the promoter sequence that
10 comprises a variable sequence that varies within the library,
11 wherein a same cis element sequence is employed with a given
12 reporter sequence within the library of constructs,
13 forming mRNA transcription products by those of the transduced or
14 transfected cells of the known cell type in which an activated transcription factor is
15 present that binds to the cis element of the construct present in the cell and activates
16 transcription of the reporter sequence of the construct present in the cell,
17 determining which reporter sequences are comprised within the mRNA
18 transcription products, and
19 determining which activated transcription factors are present in the cell
20 sample of the known cell type based on which reporter sequences were transcribed.

1 36. A method according to claim 33 wherein the library of constructs comprises
2 at least 10 different reporter sequences.

1 37. A method according to claim 33 wherein the library of constructs comprises
2 at least 20 different reporter sequences.

1 38. A method according to claim 33 wherein the library of constructs comprises
2 at least 50 different reporter sequences.

1 39. A method for diagnosing a disease state in a cell sample, the method
2 comprising:

3 identifying multiple different activated transcription factors in a cell sample
4 by
5 transducing or transfecting a cell sample to comprise a library of
6 constructs, each construct comprising
7 a cis element sequence comprising one or more copies of a cis
8 element to which a transcription factor is capable of binding, the cis element
9 sequence varying within the library of constructs,
10 a promoter sequence 3' relative to the cis element sequence,
11 and
12 a reporter sequence 3' relative to the promoter sequence that
13 comprises a variable sequence that varies within the library,
14 wherein a same cis element sequence is employed with a
15 given reporter sequence within the library of constructs,
16 forming mRNA transcription products by those of the transduced or
17 transfected cells in which an activated transcription factor is present that binds to the
18 cis element of the construct present in the cell and activates transcription of the
19 reporter sequence of the construct present in the cell,
20 determining which reporter sequences are comprised within the
21 mRNA transcription products, and
22 determining which activated transcription factors are present in the
23 cell sample based on which reporter sequences were transcribed; and
24 comparing the combination of multiple different activated transcription
25 factors identified as being present in a cell sample to combinations of multiple
26 different activated transcription factors known to be present in diseased and healthy
27 cell samples.

1 40. A method according to claim 39 wherein the library of constructs comprises
2 at least 10 different reporter sequences.

1 41. A method according to claim 39 wherein the library of constructs comprises
2 at least 20 different reporter sequences.

1 42. A method according to claim 39 wherein the library of constructs comprises
2 at least 50 different reporter sequences.

1 43. A method for screening for transcription factor modulators, the method
2 comprising:

3 taking a cell library comprising a library of constructs, each construct
4 comprising

5 a cis element sequence comprising one or more copies of a cis
6 element to which a transcription factor is capable of binding, the cis element
7 sequence varying within the library of constructs,

8 a promoter sequence 3' relative to the cis element sequence, and

9 a reporter sequence 3' relative to the promoter sequence that

10 comprises a variable sequence that varies within the library of constructs,

11 wherein a same cis element sequence is employed with a given
12 reporter sequence within the library of constructs;

13 exposing the cell library to one or more different agents;


14 forming mRNA transcription products by those cells in the library in which
15 an activated transcription factor is present that binds to the cis element of the
16 construct present in the cell and activates transcription of the reporter sequence of
17 the construct present in the cell;

18 determining which reporter sequences are comprised within the mRNA
19 transcription products for the cells exposed to the different agents; and

20 determining changes in transcription factor activity in response to the cells
21 being exposed to the one or more different agents based on which reporter sequences
22 were transcribed.

1 44. A method according to claim 43 wherein the library of constructs comprises
2 at least 10 different reporter sequences.

1 45. A method according to claim 43 wherein the library of constructs comprises
2 at least 20 different reporter sequences.

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- 1 46. A method according to claim 43 wherein the library of constructs comprises
 - 2 at least 50 different reporter sequences.

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